Psychotherapeutic process of cognitive-behavioral intervention in HIV-infected persons: Results from a controlled, randomized prospective clinical trial

Znoj, H J ; Messerli-Bürgy, Nadine ; Tschopp, S ; Weber, R ; Christen, L ; Christen, S ; Grawe, K

Abstract: The aim of this exploratory study was to examine the possible mechanisms of behavioral change in a cognitive-behavioral intervention supporting medication adherence in HIV-infected persons. A total of 60 persons currently under medical treatment were randomized to psychotherapy or usual care and were compared with a sociodemographically matched group of general psychotherapy clients. Outcome measures included therapy adherence using medication event-monitoring system psychotherapeutic processes and changes of experience and behavior. The general psychotherapy group was initially more distressed than HIV psychotherapy patients and reached higher levels of psychotherapeutic effect. In the HIV psychotherapy patients, a significant effect was found for maintaining adherence to medical treatment (Weber et al., 2004). These findings show that psychotherapy is a beneficial intervention for HIV-infected persons, and therapeutic alliance and activation of resources do not differ from a general psychotherapy treatment. Differential effects were detected for specific process variables, namely problem actuation.

DOI: https://doi.org/10.1080/10503300903246663

Psychotherapy Research, March 2010; 20(2): 203–213

Routledge
Taylor & Francis Group

Psychotherapeutic process of cognitive–behavioral intervention in HIV-infected persons: Results from a controlled, randomized prospective clinical trial

HANS-JÖRG ZNOJ[1], NADINE MESSERLI-BURGY[1], SIMONE TSCHOPP[1], RAINER WEBER[2], LISANNE CHRISTEN[3], STEPHAN CHRISTEN[3], & KLAUS GRAWE[1†]

[1]*Department of Psychology, University of Bern, Bern, Switzerland;* [2]*Division of Infectious Disease and Hospital Epidemiology, University Hospital, Zurich, Switzerland &* [3]*Arbeitsgemeinschaft Sozialwissenschaft Gesundheitsforschung Informatik, Uetikon, Switzerland*

(Received 19 June 2007; revised 28 July 2009; accepted 7 August 2009)

Abstract

The aim of this exploratory study was to examine the possible mechanisms of behavioral change in a cognitive–behavioral intervention supporting medication adherence in HIV-infected persons. A total of 60 persons currently under medical treatment were randomized to psychotherapy or usual care and were compared with a sociodemographically matched group of general psychotherapy clients. Outcome measures included therapy adherence using medication event-monitoring system psychotherapeutic processes and changes of experience and behavior. The general psychotherapy group was initially more distressed than HIV psychotherapy patients and reached higher levels of psychotherapeutic effect. In the HIV psychotherapy patients, a significant effect was found for maintaining adherence to medical treatment (Weber et al., 2004). These findings show that psychotherapy is a beneficial intervention for HIV-infected persons, and therapeutic alliance and activation of resources do not differ from a general psychotherapy treatment. Differential effects were detected for specific process variables, namely problem actuation.

Keywords: HIV; cognitive–behavioral intervention; psychotherapeutic process; adherence; mechanisms of change

Maintaining adherence is one of the major challenges in HIV-infected patients (Paterson et al., 2000). Viral resistance can develop when drug levels are insufficient to stop viral replication completely. Drug resistance may lead to clinical progression in the individual, and resistant organisms can be transmitted to other persons. Yet adherence to drug therapy for a chronic and incurable illness is demanding for patients.

The World Health Organization has launched a campaign to promote therapy adherence in the treatment of chronic diseases (Sabaté, 2003). Definitions of adherence following Bissonnette (2008) have been conceptualized in different ways among the disciplines of medicine, psychology, and pharmacy. In the case of HIV-infected participants, the medical approach has been taken. It is highly important for participants to meticulously follow the instructions of the pharmacological treatment. Thus, the focus of the psychological intervention has to be on difficulties or personal barriers in order to improve adherence to therapy.

Numerous predictors of adherence have been recognized, including physician–patient communication, organizational aspects of care settings, patient characteristics (e.g., emotional issues, health status, sociodemographic and behavioral variables, and recreational drug use), mode of drug regimen (e.g., number of pills, dosing frequency; Nieuwkerk & Oort, 2005), and adverse treatment events such as side effect severity (Mannheimer, Friedland, Matts, Child, & Chesney, 2002; Turner, 2002). In particular, depression, self-efficacy, and social support were shown to distinguish between good and poor adherence (Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000). Maintaining long-term treatment can be particularly challenging when the treatment course develops other than as expected, adverse blood results occur, or patients suffer from other side effects of the treatment. We assume that the fundamental

Correspondence concerning this article should be addressed to Hans-Jörg Znoj, University of Bern, Department of Psychology, Gesellschaftsstrasse 49, 3012 Bern, Switzerland. E-mail: hansjoerg.znoj@psy.unibe.ch
†Deceased.

ISSN 1050-3307 print/ISSN 1468-4381 online
DOI: 10.1080/10503300903246663

precondition for maintenance of drug therapy is the patient's motivation and his or her readiness for a behavior change (Prochaska, DiClemente, & Norcross, 1992; Weber et al., 2004).

The impact of social support on enhancing quality of life and adherence to medication in HIV-infected persons has been investigated already (Gonzalez et al., 2004; Simoni, Frick, Lockhart, & Liebovitz, 2002). However, only scant support for specific interventions has been found (Fogarty et al., 2002; Haddad et al., 2000; Haynes, McDonald, Garg, & Montague, 2002; Haynes, McKibbon, & Kanani, 1996; McDonald, Garg, & Haynes, 2002). Recently published data have shown some effects of group cognitive–behavioral therapy (CBT) on changes in risk behavior (Kalichman, Rompa, & Cage, 2005), depressive symptoms, and social support (Carrico, Antoni, Weaver, Lechner, & Schneiderman, 2005) and modest effects on adherence (Wagner et al., 2006): First results of an individual psychotherapy intervention showed significant effects on adherence, as discussed in Weber et al. (2004). No data exist on meaningful factors or combination psychotherapy for successful behavior change. A better understanding of these factors could even help to maintain or enhance medication adherence among persons who do not seek psychotherapy. Additionally, knowledge of how such intervention differing from a psychotherapeutic process seems to be important in terms of treatment improvements in HIV patients.

In general, psychotherapy to support behavior change is based on several general principles. Grawe (1997, 2004b) postulated four research-informed mechanisms of change: mastery/coping, clarification of meaning, problem actuation, and resource activation. All of these mechanisms of change might be linked to outcome and be dependent on distinctly different psychotherapeutic goals (i.e., supporting adherence to therapy for HIV-infected persons vs. reducing psychopathology in individuals receiving outpatient psychotherapy).

In the first proposed mechanism of change—mastery/coping—the patient and therapist approach the problem in terms of ability. Therapeutic skills and an appropriate understanding of the patient's problem are essential for progress. In the second mechanism—clarification of meaning—feelings (following Lazarus's, 1991, appraisal theory of emotion) are changed by approaching whatever the patient sees as a threat to a personal goal in terms of its motivational components (i.e., approach vs. avoidance). Clarifying the meaning of a specific situation or altering the importance of a personal goal may change the patient's feelings dramatically (Greenberg, Rice, & Elliott, 1996). The third proposed mechanism of behavior change is problem actuation, which is based on the insight that automated behavior and perception can be changed only by activating the neural foundation, that is, by experiencing avoided situations. The fourth, and possibly the most important, factor in effecting change are the patient's own resources; psychotherapy can only work with what the patient brings into therapy. Resources such as strong motivation, social resources, verbal capacity, and imagination are necessary ingredients for therapeutic change (Gassmann, 2002).

Within this framework, the objectives of our 1-year randomized trial were twofold: (a) to study patients' reported changes in experience and behavior and investigate the mechanisms of behavior change linked to maintenance of adherence, and (b) to compare the dose–effect relationship for the proposed mechanisms of change in the HIV psychotherapy group and an age- and gender-matched sample of psychotherapy patients in an outpatient setting (general psychotherapy group).

Materials and Method

Participants

HIV-infected patients. Of 60 randomized HIV-infected persons originally recruited, we were able to analyze data from 53. Seven patients did not finish the trial. One patient was erroneously randomized, five dropped out during the study, and one died (unrelated to the study). The final sample included 43 men (81.1%) and 10 women (18.9%) ranging in age from 25 to 71 years ($M = 44.3$, $SD = 10.7$). Twenty-nine were allocated to the standard of care plus psychotherapy group (HIV psychotherapy group), including 21 men (72.4%) and eight women (27.6%) ranging in age ranged from 25 to 71 years ($M = 44.8$, $SD = 11.1$). One participant did not complete the questionnaires. Twenty-four participants were allocated to the standard-of-care control group (HIV control group), including 22 men (91.7%) and 2 women (8.3%) ranging in age from 31 to 65 years ($M = 43.7$, $SD = 10.5$). The allocation schedule for the two treatment arms and three different CD4 strata (0–0.05×10^9/l, 0.051–0.2×10^9/l, or $> 0.2 \times 10^9$/l), with randomly permuted block sizes of two and four, was generated in advance with the program RANCODE V 3.0 (IDV Datenanalyse und Versuchsplanung, Gauting, Germany) and properly concealed from care providers. CD4 is an indicator of the degree of HIV infection and was used in this study to stratify the treatment arms. CD4 is a primary receptor used by HIV-1 to gain entry into host T cells.

General psychotherapy patients. A group of 28 patients from a psychotherapeutic ambulatory facility (outpatient clinic of the University of Bern,

Switzerland) matched on sociodemographic factors (age and gender) formed a comparison group for the intervention arm of the HIV-infected persons (psychotherapy). The participants in this group suffered from a variety of psychopathological disorders, mainly anxiety disorders (~50%) and depression (~30%). In contrast to the HIV group, members of the comparison group had chosen psychotherapeutic treatment of their own accord or had been recommended for psychotherapy by health authorities. The participants of this group included 21 men and seven women ranging in age from 31 to 62 years ($M = 40.6$, $SD = 7.9$). The mean number of sessions for members of the comparison group was 33.2 ($SD = 17.3$, range 11–77).

In the beginning, members of the general psychotherapy group had higher levels of distress ($M = 1.03$, $SD = 0.52$) than the HIV psychotherapy group, as measured with the Symptom Checklist-90-Revised (SCL-90-R) Global Severity Index (GSI). The mean pretreatment GSI was 0.55 ($SD = 0.39$) for participants receiving psychotherapy ($N = 29$) and 0.42 ($SD = 0.47$) for controls ($N = 24$). There was no posttreatment (i.e., after 12 months) difference between groups. Goal attainment scaling was used to identify personal therapeutic goals in the HIV-infected group as well as in the matched general psychotherapy group. For the HIV intervention group the principal therapeutic goal was adherence to therapy. This principal goal had to be the main focus of their therapeutic intervention. Additional individual goals might have been formulated individually. In contrast, for the matched general psychotherapy group, the principal outcomes were assessed individually in terms of each person's major complaint without any restrictions in terms of treatment goals.

Therapists

Intervention was provided by licensed psychotherapists in private practice. All of them had formal training in CBT, had heard a 2-hr lecture on antiretroviral therapy before the study, and were instructed to focus on the maintenance of antiretroviral drug adherence. They were free to work as they saw fit on any other problem the patient presented to them. The sessions were all tape-recorded and psychotherapists were closely supervised.

Design

We conducted a prospective, controlled 12-month trial with 60 HIV-infected persons on antiretroviral combination therapy who were 1:1 randomized to receive standard of care or standard of care plus individual cognitive–behavioral intervention provided by psychotherapists. Study design and patient selection have been described elsewhere (Weber et al., 2004). Inclusion criteria were as follows: antiretroviral therapy containing a combination of at least three different drugs of at least two different drug classes, viral load below 50 copies/ml, participation in the Swiss HIV cohort study, and no intravenous drug use (or, in case of drug addiction, on stable methadone maintenance). Ethics committee approval was obtained, and all participants gave written informed consent. Standard of care and study consultations of each patient were provided by the same physician at the University Hospital HIV outpatient clinic in Zurich, Switzerland. After randomization, participants in the intervention arm received the address of one of the psychotherapists and were asked to schedule a first appointment. The allocation of participants to psychotherapists was random, based on the number of participants each psychotherapist indicated before the start of the study that they would care for. The study protocol specified a minimum of three and a maximum of 25 sessions within the 1-year study period. Within these bounds, appointment frequency was worked out by participants and psychotherapists during the course of the study. Intervention sessions lasted 45 min on average. The mean number of sessions per participant was 12.8 ($SD = 6.8$). Participants were informed that the intervention was not proposed to address a psychological problem or psychiatric disease but rather to support adherence to drug therapy using CBT.

Psychotherapists were instructed to define at first visit, together with the participants, at least two goals for future intervention. At least one of these goals had to be related to adherence to antiretroviral therapy, but participants and psychotherapists were free to identify additional goals not related to HIV therapy. Interventions had to be based on concepts of CBT (Bandura, 1977).

Measures

Adherence measure. Medication intake in the intervention and control groups was assessed using the eDEM medication event-monitoring system (Aardex Ltd., Zug, Switzerland; Cramer, Mattson, Prevey, Scheyer, & Quellette, 1989). The study nurse working closely with the physician downloaded the monitoring data monthly to a central database in the presence of the participants, who saw their own performance on screen as a graphic, depicting times at which pillboxes were opened during the previous month. We used the measurements for the first month of the study to approximate baseline values.

Psychosocial measures. The German translation of Derogatis's SCL-90-R (Franke, 1995), a structured and standardized questionnaire, was used at

baseline and at 12 months to screen for nine symptoms of psychopathology (e.g., depression, anxiety) and to measure GSI, intensity of symptoms, and number of self-reported symptoms. Baseline measurements from these instruments were evaluated using a computer program and the results transferred at once to the appropriate psychotherapists. Compared with a group of healthy individuals (Franke, 1995), mean GSI was slightly higher in our HIV group; however, mean values were lower than in a comparable group of HIV-infected persons (Franke, Jäger, & Stäcker, 1995). Psychometrically, the SCL-90-R showed excellent reliability in the HIV sample (Cronbach's $\alpha = .94$).

The structured and standardized questionnaire Veränderungsfragebogen des Erlebens und Verhaltens (VEV-VW; Zielke & Kopf-Mehnert, 1978; Willutzki, 1999) was used at 6 and 12 months to assess changes of experience and behavior as perceived by participants themselves. The questionnaire consisted originally of 27 bipolar items that are answered on a 7-point Likert scale (e.g., "I am more relaxed" vs. "I am more tense"). The total score is indicative of "quietness, confidence, optimism" versus "stress, uncertainty, pessimism" (Weber et al., 2004). For the present study, the VEV questionnaire was reduced to 17 items. Psychometrically, the shortened VEV showed excellent reliability in the HIV sample (Cronbach's $\alpha = .96$).

Therapy process assessment. Psychotherapists kept a record on qualitative information and used goal attainment scaling (Kiresuk & Lund, 1978) to identify intervention goals. Therapeutic process was assessed by a theory-driven postsession report (Regli & Grawe, 2000) completed by therapists and patients independently. Items on the postsession report were formulated according to the four postulated mechanisms of change (Grawe, 1997). Additional items examined progress made during the session.

An example item in the mastery/coping category for patients is "I feel competent in situations I didn't feel competent in until now." The same category was rated by the therapists in response to such items as "Today, I have actively worked on helping the patient to cope with situations that are difficult for him or her to handle." Reliabilities of patient and therapist scales differed greatly. Cronbach's α ranged from .16 to .77 for patients and from .26 to .93 for therapists. Because both patients and therapists focused on the same change mechanisms, we built a single scale using the two perspectives. For reliabilities of the combined scales, see Table I.

For patients, clarification of meaning included such items as "Today possible solutions for my problems (fulfillment of wishes, reaching my goals) have been clarified." For therapists, a typical item was "I have actively aimed at helping the patient to see new connections in relation to his or her problems (needs and goals)." For patients, problem actuation included such items as "What we covered in today's session was at times very unpleasant." For therapists, a typical item was "Today I aimed deliberately at involving the patient's feelings." Patient resource activation items included, for example, "Right now I feel supported by the therapist in the way I like to be." For therapists, a typical item was "In today's session I have actively tried to activate and specifically use the patient's resources." Therapeutic alliance is seen as a specific resource within the psychotherapy situation. For patients, an exemplary item on this scale was "Today I felt comfortable in the relationship with the therapist." Most items were negatively labeled, as, for example, "I believe that the therapist could attend more to my feelings." For therapists, items included statements like "Today I felt comfortable in the relationship with the patient." The postsession reports for both patient and therapist included a scale for felt therapeutic progress. The patient postsession report also included items for corrective experiences and self-efficacy.

Statistics

Statistical analysis was performed using parametric methods for comparisons of independent and dependent samples. To identify time trends in adherence as measured by medication event-monitoring system, we calculated a slope for each patient using linear regression. We then tested whether adherence slopes for patients from the intervention and control groups differed from each other (analysis of variance repeated measurement design). We used correlations as a measure of association. Additionally, reliability scores for the process scales were calculated separately for HIV participants and outpatient psychotherapy participants (see Table I). To improve reliability, patient and therapist perspectives were taken together. Means and standard deviations reflect the combined perspective in Table I.

Results

Effects of Psychological Intervention

Of the 23 persons in the psychotherapy treatment group who completed psychotherapeutic treatment, 16 maintained initial high medication adherence. In the control group, only five of 24 maintained initial high adherence.

Apart from the positive effect of psychotherapy on adherence (see Weber et al., 2004), a major effect on changes of experience and behavior, such as feeling

Table I. Descriptives and Reliability of Process Variables Measured by Postsession Report

	HIV psychotherapy ($n=28$)		General psychotherapy ($n=28$)	
Process variable (no. items)	*M* (*SD*)	α	*M* (*SD*)	α
Mastery/coping (4)	−0.33 (0.56)	.73	0.35 (0.48)	.74
Clarification of meaning (6)	−0.30 (0.63)	.81	0.26 (0.58)	.66
Problem actuation (5)	−0.53 (0.54)	.81	0.63 (0.51)	.76
Resource activation (6)	−0.15 (0.77)	.86	0.07 (0.64)	.79
Therapeutic alliance (4)	−0.12 (0.77)	.68	0.00 (0.71)	.82
Progress in therapy (3)	−0.50 (0.76)	.74	0.44 (0.40)	.61
Corrective experiences (5)	−0.41 (0.86)	.83	0.35 (0.58)	.81
Self-efficacy (3)	−0.55 (0.79)	.77	0.45 (0.62)	.73

Note. Means and standard deviations are calculated for *z*-transformed data to obtain the same metric for the two samples (pooled sample from all measurements). The variables corrective experiences and self-efficacy were scales of the patient postsession report, so only the patient's perspective is represented by these variables. The other process variables are combined values of therapist and patient perspectives.

more confident and relaxed, more optimism, and a better sense of coming to terms with their problems, $F(1, 53) = 6.81$, $p = .01$, was found. Moreover, the total score of changes of experience and behavior correlated significantly with adherence slope ($r = 0.29$, $p < .05$), and participants with better adherence improved more reliably in experience and behavior. Participants with 10 or more cognitive behavior interventions experienced more improvement; these results were presented and discussed in Weber et al. (2004). A comparison of the two median-split groups (improved adherence and not improved adherence) revealed a significant difference between them, $F(1, 38) = 9.16$, $p < .01$.

Psychotherapy Process in the HIV Psychotherapy Group

Table II shows the product–moment correlations between changes of experience and behavior and measures of process such as therapeutic alliance, activation of resources, and clarification of meaning. For this purpose, the process measures have been averaged over the entire course of each individual treatment. Therefore, the correlations in Table II do not show process over time but global association with changes of experience and behavior. These correlations in the table suggest that the associations between process variables and variables of micro-outcome strengthen over the course of treatment with the global outcome, as measured with the VEV. However, this is not the case for some process variables. The strongest effect is on corrective experiences, a clear measure of micro-outcome.

Our main hypothesis was that participants of the psychotherapy treatment group, who experienced more improvement in adherence and changes of experience and behavior, would also show higher levels of involvement in therapeutic process, as measured by the four process variables. Accordingly, we median-split the psychotherapy group sample by high versus low changes of experience and behavior (low VEV and high VEV) at the end of therapy into not improved (low VEV) and improved (high VEV) and tested against the course of the process variables. The course of the psychotherapy was aggregated into three phases, following Howard and others (Howard, Orlinsky, & Lueger, 1994; Hill & Lambert, 2004). This was necessary because of the large differences in treatment length and number of sessions. As a

Table II. Correlations of Process Variables and Variables of Micro-Outcome with Change of Experience and Behavior (VEV) at the End of Therapy in the HIV Psychotherapy Group

Process variable	Phase 1	Phase 2	Phase 3	Whole therapy
Mastery/coping	.12	.32	.65**	.49*
Clarification of meaning	.41*	.18	.54**	.48**
Problem actuation	.03	.15	.13	.00
Resource activation	.42*	.48*	.45*	.50**
Therapeutic alliance	.28	.41*	.24	.35
Progress in therapy	.45*	.56**	.50**	.55**
Self-efficacy	.05	.48*	.40*	.36
Corrective experiences	.32	.40*	.70**	.53**

Note. $N = 28$. Phases 1 to 3 represent the course of psychotherapy divided into three phases. Whole therapy denotes the average over all phases and represents the degree of association of the process variables with change at the end of therapy. VEV = Veränderungsfragebogen des Erlebens und Verhaltens.
*$p < .05$. **$p < .01$.

baseline for each patient, we used the values of the first session.

Therapeutic alliance did not differ between the improved and not-improved groups, and there was no effect for course or interaction between course and group for therapeutic alliance. Activation of resources tended to separate the two outcome groups, $F(1, 25) = 3.30$, $p < .10$, $\eta^2 = .12$, but there was no effect for course or any interaction between groups and time course. For clarification of meaning, there was a tendency for an effect between groups, $F(1, 25) = 2.74$, $p = .11$, $\eta^2 = .10$, and for an effect of time course, $F(1, 25) = 3.90$, $p < .10$, partial $\eta^2 = .14$, indicating a negative slope toward the end of therapy in both groups. For mastery/coping, there was no main effect between the two groups but a trend for a statistical interaction between time course and VEV outcome, $F(1, 25) = 3.51$, $p < .10$, partial $\eta^2 = .12$. The latter indicated that the HIV patients who gained more in the psychotherapeutic treatment improved in mastery/coping, as seen by both themselves and therapists, in contrast to the not-improved group. For problem actuation, we found no differences between the two groups.

Micro-outcomes (i.e., corrective experiences and self-efficacy, as reported by the patient, and progress in therapy, as rated by patients and therapists) also separated the two groups, indicating that patients and therapists were good judges of the ongoing process. For corrective experience, this effect was highly significant between the improved and not-improved groups, $F(1, 25) = 8.23$, $p < .01$, partial $\eta^2 = .25$, and there was an additional interaction effect between the outcome groups and time course, $F(1, 25) = 3.29$, $p < .01$, partial $\eta^2 = .12$. Progress in therapy also separated the two groups, $F(1, 25) = 6.16$, $p < .05$, partial $\eta^2 = .20$. There was an expected interaction tendency in that persons in the improved outcome group also reported more self-efficacy in the course of the psychotherapeutic intervention, $F(1, 25) = 2.77$, $p < .10$, partial $\eta^2 = .10$. Figure 1 (A–D) shows the reported effects between the two outcome groups of HIV-infected persons in the four proposed process variables.

Comparison of HIV Psychotherapy and General Psychotherapy Groups

A comparison of psychological outcome measures confirmed two effects: Patients in the general psychotherapy group (a) were initially more distressed, as measured with the SCL-90-R GSI, and (b) reached higher levels of effect (pre–post) compared with those in the HIV psychotherapy group.

The outpatient group completed the same post-session reports as the main study group, and we felt that we could compare the process variables. However, it should be noted that the average duration of therapy for the outpatient group was more than 30 sessions compared with 13 sessions for the HIV-infected group.

We hypothesized that in self-referred psychotherapy (the outpatient clinic group) the mechanisms of change would be more pronounced and result in greater change. In Table III, group comparisons for the five mechanisms of change (counting therapeutic alliance) and the three micro-outcomes (progress in therapy, corrective experiences, and self-efficacy) are given.

Figure 2 (A–D) depicts the averaged phases in the four process variables for the main and comparison groups. Although all differences were in the predicted direction, the effect on problem actuation was larger than expected. There were no differences between the two groups in terms of resource activation and therapeutic alliance. The differences between the two groups over the course of treatment included the first session (baseline), with the exception of clarification of meaning, for which there was one significant interaction (Group $\times$ Time Course). Again, the direction of the effect was as expected: Over the course of treatment, outpatients choosing psychotherapy reported more clarification of meaning than those randomly assigned to psychotherapy in the main study group.

Discussion

We studied the relationship between adherence and change of experience and behavior. Furthermore, we were interested in the postulated mechanisms of change and outcome in HIV-infected patients during psychotherapy. We hypothesized that adherence and change of experience are related. We observed that the change of experience and behavior was associated with improved adherence. Therefore, psychotherapy might be a beneficial intervention for HIV-infected persons undergoing a challenging drug treatment. This result enhances and builds upon the finding of Weber et al. (2004) of a significant relationship between adherence and psychotherapy. Furthermore, members of the HIV psychotherapy group reported greater improvement in their mental health and behavior during the study period than did members of the HIV control group. This improvement correlated with number of sessions (i.e., patients having 10 or more consultations with a psychotherapist reported more improvement than those who had fewer). The cost of the additional intervention approximates the cost of 1 month of the standard triple-antiviral regimen (Weber et al., 2004).

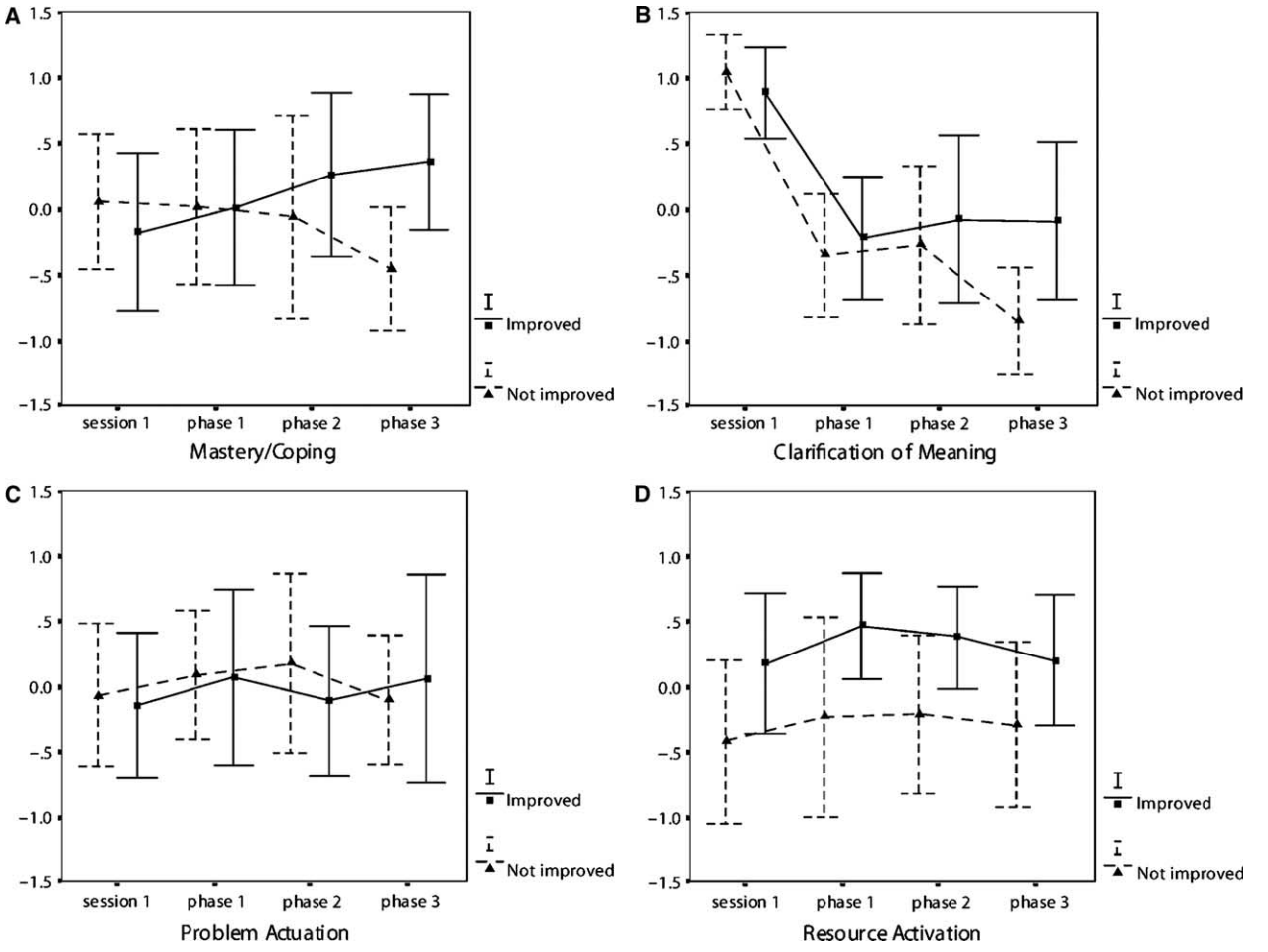

Figure 1. (A–D) The *z*-transformed scores of four process variables for the HIV psychotherapy group in the randomized trial median-split with high and low changes in experience and behavior (Veränderungsfragebogen des Erlebens und Verhaltens). The first session is the baseline; the three phases are average scores for sessions in the beginning, middle, and end phases of therapy.

More specifically, we hypothesized that HIV-infected patients with improvements in adherence and changes of experience and behavior show higher levels of involvement in therapeutic process. We observed that almost all proposed mechanisms of therapy such as mastery/coping, clarification, resource activation, and therapeutic alliance correlated with both medication adherence and perceived improvement in mental health and behavior. However, detailed results of involvement in therapeutic process measured by four process variables—therapeutic alliance, activation of resources, clarification of meaning, and mastery/coping—were rather inconsistent. When the intervention group was separated into those who perceived high mental health and behavior benefit (improved group) and those who perceived low benefit (not improved), analysis suggests that the former were more deeply involved in the psychotherapeutic process and, therefore, benefited from higher levels of the proposed mechanisms of change. This effect could not be attributed to therapeutic alliance: Patients and therapists of both the improved and the not-improved groups rated the quality of the therapeutic alliance at about the same level. As a result of relatively small sample sizes, it must be considered that results could reflect a Type II error (β error). Additionally, the exploratory approach in this study has to be considered. Nonsignificant findings should not be interpreted because of weak power, whereas significance might be effected by exploratory multiple testing and, therefore, should be interpreted with caution.

Furthermore, in comparing the HIV-infected psychotherapy group and an outpatient clinic group of individuals with self-referred psychotherapy, we hypothesized that mechanisms of change would be more pronounced and result in greater change in the latter. We observed that the two groups did not differ in basic ingredients of psychotherapeutic change such as therapeutic alliance and activation of resources in contrast to problem actuation. These results seem to indicate an important message: In order to change patterns of problematic behavior and experience, problems have to be activated. Hence,

Table III. Results of the Analysis of Variance Repeated Measurement Design of Process Variables Comparing the HIV Psychotherapy Group ($n = 28$) and the Demographically Matched General Psychotherapy Group ($n = 28$)

Process variable	*F*	*df*	η^2
	Between-subject effects		
Mastery/coping	24.12**	1, 54	.31
Clarification of meaning	11.86**	1, 54	.18
Problem actuation	67.03**	1, 54	.55
Resource activation	1.32	1, 54	.02
Therapeutic alliance	0.38	1, 54	.01
Progress in therapy	33.65**	1, 54	.38
Corrective experiences	14.93**	1, 54	.22
Self-efficacy	27.84**	1, 54	.34
	Interaction effects (Time Course × Group)		
Mastery/coping	0.50	2,108	.02
Clarification of meaning	3.85*	1.86,[a] 108	.07
Problem actuation	0.20	2, 108	.01
Resource activation	1.46	2, 108	.05
Therapeutic alliance	0.93	1.66,[a] 108	.01
Progress in therapy	2.01	2, 108	.07
Corrective experiences	0.37	2, 108	.01
Self-efficacy	1.06	1.69,[a] 108	.02

Note. Within effects were suppressed for this table.
[a]With Huynh–Feldt correction.
*$p < .05$. **$p < .01$.

problem actuation will occur only with sufficient motivation for psychological change. Further, we would expect mastery/coping and clarification of meaning to occur simultaneously, and this is indeed what the data suggest: Both these process variables differ largely between the two groups, again in the expected direction. Likewise, the micro-outcomes, as judged by patients and therapists, differed highly significantly between the two groups, showing medium to large effect sizes. The differences in motivation for treatment and amount of psychological distress during pretreatment do not reduce these findings.

Adherence to medication is an immense task: Not only must one swallow many pills a day (often more than 10), but some of these pills have to be refrigerated, some taken before meals, some after, and some at regular times each day. An HIV-positive person often has other difficulties as well (Folkman, 1997), such as facing the illness and death of loved ones. Results of our study suggest that supportive intervention, especially clarification of meaning, can improve quality of life for HIV-infected persons. By helping patients focus on new relations and new perspectives, therapists can actively turn "lead into gold" (Taylor & Brown, 1988), installing a positive feedback loop that helps them maintain good humor, high self-esteem, and good affect regulation. In particular, an intervention based on cognitive–behavioral techniques seems to help HIV-infected persons maintain high medication adherence.

Limitations

To our knowledge, this is the first study to assess the process of behavioral change in a randomized controlled trial involving HIV-infected persons. The change aimed for was maintaining medication adherence, which limits the cognitive–behavioral intervention to a single problem. The randomized design did not account for clinical considerations or the individual needs of patients. However, participants in the intervention arm were free to quit the additional treatment as they wished. The average number of sessions was relatively low considering that patients were not charged for therapy (weekly individual sessions) and were free to discuss further personal problems in addition to adherence. However, nobody quit, and some patients attended the maximum number of sessions.

The relatively large range of participation in the intervention group posed problems in terms of process research. We followed a rather simple rule, dividing all interventions into three parts or phases: beginning, middle, and end of psychological intervention. Another difficulty was assessment of process variables. There is a large and still growing body of literature concerning the question of the process–outcome relationship in psychotherapy (Orlinsky, Rønnestad, & Willutzki, 2004). We solved this problem by using a theory-driven measurement of postsession reports completed both by therapist and patient to obtain reliable scales of clinically relevant psychotherapy process variables (Lambert & Ogles,

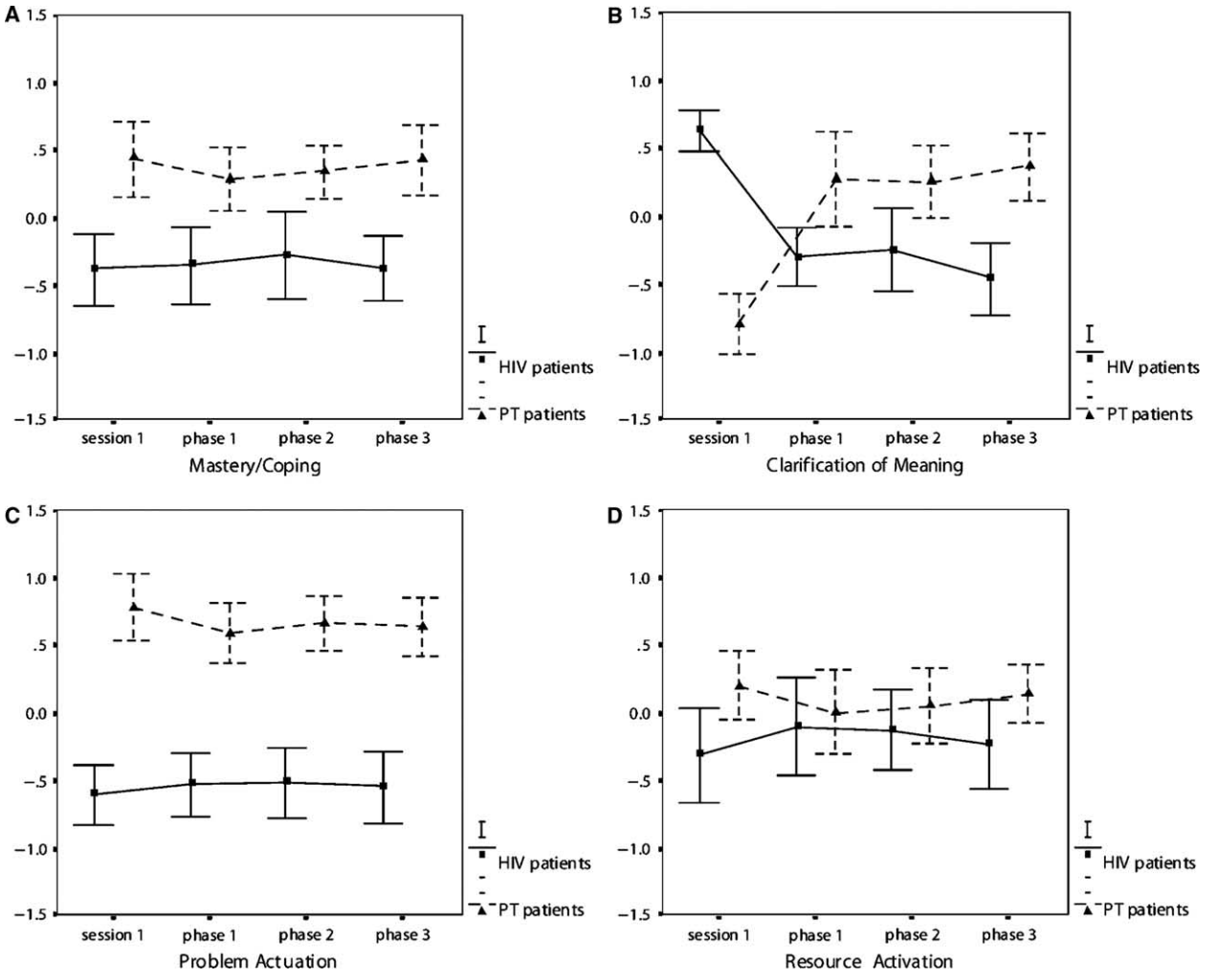

Figure 2. (A–D) The *z*-transformed scores of the process variables in the HIV psychotherapy (PT) group and in the general psychotherapy group. The first session is the baseline; the three phases are average scores for sessions in the beginning, middle, and end phases of therapy.

2004). Orlinsky and Howard (1978) have stressed the importance of an experiential perspective on the events of therapy. By using self-report, we emphasize the experience of both patients and therapists rather than "objective" observer criteria. The postsession report used in this study had been revised several times, gradually integrating scales for change mechanisms (Grawe, 2004b).

We focused on mastery/coping, clarification of meaning, and problem actuation as mechanisms of change. Arguably, other variables are also involved in psychotherapy, such as emotional regulation mechanisms (Mergenthaler, 1996; Znoj, Nick, & Grawe, 2004), motivational processes (Jeger, Znoj, & Grawe, 2003; Schulte, Hartung, & Wilke, 1997; Znoj et al., 2000), and cognitive processes such as assimilation of problematic experiences (Stiles, 2002).

The method of measuring mechanisms of change used here has the advantage of not requiring great research investment; combining the perspectives of patient and therapist creates relative objectivity. The process variables in this study have theoretically been linked to the outcome (Grawe, 2004a), but it is unclear to what extent these process variables might influence each other. There is a strong body of evidence that these variables are not independent. For instance, Gassmann (2002) showed that a strong focus on problem activation without resource activation leads to an impaired session outcome and that the interplay between these two variables is important for the outcome of psychotherapy. Our focus in this study was mainly to show that the postulated process variables are linked to the outcome. The results in the primary study, which showed differential use of change mechanisms, were confirmed in the comparison study. Most interestingly, the so-called basic requirements of psychotherapy—working alliance and resource activation—were not observed to differ in the two studies. We focused on change of experience and behavior (VEV) as the main outcome measure because the HIV treatment group showed very low signs of psychological disturbances

as rated by the SCL-90-R. This fact limits the possible improvements resulting from psychological interventions.

In the first analysis there was a trend indicating that the improved subgroup of HIV-infected persons experienced more resource activation during the sessions; however, in contrast to our assumptions, in the HIV intervention group problem actuation was not related to outcome. This could be due to the relatively low psychological distress of the HIV-infected persons in this study. In fact, the GSI for participants in this study was even lower than in a normative sample of HIV-infected men (Franke et al., 1995). This might be a result of the highly effective medication treatment administered to participants in the present study. It is important to stress that all participants in the study were selected randomly (Weber et al., 2004).

A limitation of this study concerns the manipulation check and treatment in general. There was no systematic manipulation check in this study. However, all therapists of the HIV intervention group were supervised in terms of the main treatment goals, namely improvement of the adherence to medical therapy. The small sample size of the HIV intervention group and the post hoc approach that was followed in this research reduce the power of the presented analyses and the generalizability of the results. To our knowledge, this is the first study regarding process–outcome research in HIV patients. Therefore, an exploratory approach was appropriate. Although many of the contrasts do not reach statistic significance, the given effect sizes show that this might be due to lack of statistical power. The results of this study have to be reproduced in larger samples and in a priori research designs.

Open Questions and Future Research

The psychotherapists in this study received no instruction aside from a lecture on HIV treatment and a mandate to focus on adherence. This leaves room for improvements; for instance, more focused interventions, enhanced support, or focus on positive states of mind (Gonzalez et al., 2004) might improve effectiveness. Some individuals may need clarification of motives, fears, or a grief-related topic; others lack social support; and still others lack specific skills for maintaining medication adherence. So far, studies comparing group versus individual interventions and the various interventions for groups are lacking.

We hope that this study's focus on process will lead to more investigations of topics related to adherence. Referral to mental health specialists is a possible tool for maintaining medication adherence for people infected with HIV. Further, policymakers should note that individual psychological intervention is inexpensive compared with treating the medical consequences of nonadherence.

References

Bandura, A. (1977). Self-efficacy: Toward a unifying theory of behavior change. *Psychological Review*, *84*, 191–215.

Bissonnette, J. M. (2008). Adherence: A concept analysis. *Journal of Advanced Nursing*, *63*(6), 634–643.

Carrico, A. W., Antoni, M. H., Weaver, K. E., Lechner, S. C., & Schneiderman, N. (2005). Cognitive-behavioural stress management with HIV-positive homosexual men: Mechanisms of sustained reductions in depressive symptoms. *Chronic Illness*, *1*(3), 207–215.

Catz, S. L., Kelly, J. A., Bogart, L. M., Benotsch, E. G., & McAuliffe, T. L. (2000). Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychology*, *19*(2), 124–133.

Cramer, J. A., Mattson, R. H., Prevey, M. L., Scheyer, R. D., & Quellette, V. L. (1989). How often is medication taken as prescribed? A novel assessment technique. *Journal of the American Medical Association*, *261*, 3273–3277.

Fogarty, L., Roter, D., Larson, S., Burke, J., Gillespie, J., & Levy, R. (2002). Patient adherence to HIV medication regiments: A review of published and abstract reports. *Patient Education & Counseling*, *46*, 93–108.

Folkman, S. (1997). Introduction to the special section: Use of bereavement narratives to predict well-being in gay men whose partners died of AIDS—Four theoretical perspectives. *Journal of Personality and Social Psychology*, *72*, 851–854.

Franke, G. (1995). *Die Symptom-Checkliste von Derogatis [Derogatis's Symptom Checklist-90-R, German version]*. Weinheim, Germany: Beltz.

Franke, G. H., Jäger, H., & Stäcker, K.-H. (1995). Die Symptom-Checkliste-Liste-SCL-90-R—im Einsatz bei HIV-infizierten Patienten [The Symptom-Checklist SCL-90R—Application in HIV-infected persons]. *Zeitschrift für Differentielle und Diagnostische Psychologie*, *16*, 195–208.

Gassmann, D. (2002). *Korrektive Erfahrungen im Psychotherapieprozess. Entwicklung und Anwendung der Konsistenztheoretischen Mikroprozessanalyse KMP* [Corrective experience in psychotherapy. Development and application of the consistency-based micro-process analysis]. Bern, Switzerland: University of Bern, Institute for Psychology.

Gonzalez, J. S., Penedo, F. J., Antoni, M. H., Duran, R. E., Fernandez, M. I., McPherson-Baker, S., et al. (2004). Social support, positive states of mind, and HIV-treatment adherence in men and women living with HIV/AIDS. *Health Psychology*, *23*, 413–418.

Grawe, K. (1997). Research-informed psychotherapy. *Psychotherapy Research*, *7*, 1–19.

Grawe, K. (2004a). *Neuropsychotherapie*. Göttingen, Germany: Hogrefe.

Grawe, K. (2004b). *Psychological therapy*. Cambridge, UK: Hogrefe & Huber.

Greenberg, L. S., Rice, L. N., & Elliott, R. K. (1996). *Facilitating emotional change: The moment-by-moment process*. New York: Guilford Press.

Haddad, M., Inch, C., Glazier, R. H., Wilkins, A. L., Urbshott, G., Bayoumi, A., et al. (2000). Patient support and education for promoting adherence to highly active antiretroviral therapy

for HIV/AIDS. *Cochrane Database of Systematic Reviews*, CD001442.

Haynes, R. B., McDonald, H., Garg, A. X., & Montague, P. (2002). Interventions for helping patients to follow prescriptions for medication. *Cochrane Database of Systematic Reviews*, CD000011.

Haynes, R. B., McKibbon, K. A., & Kanani, R. (1996). Systematic review of randomized trials of interventions to assist patients to follow transcriptions for medication. *Lancet*, *384*, 383–386.

Hill, C. E., & Lambert, M. J. (2004). *Methodological issues in studying psychotherapy process and outcomes*. In M. J. Lambert (Ed.), *Bergin and Garfield's handbook of psychotherapy and behavior change* (5th ed., pp. 84–135). New York: Wiley.

Howard, K. I., Orlinsky, D. E., & Lueger, R. J. (1994). Clinically relevant outcome research in individual psychotherapy: New models guide the researcher and clinician. *British Journal of Psychiatry*, *165*, 4–8.

Jeger, P., Znoj, H. J., & Grawe, K. (2003). Increase in coherence in action control as a feature of successful psychotherapies: A sequential analytical examination of the therapist–patient interaction. *Psychotherapy Research*, *13*, 415–428.

Kalichman, S. C., Rompa, D., & Cage, M. (2005). Group intervention to reduce HIV transmission risk behavior among persons living with HIV/AIDS. *Behavior Modification*, *29*, 256–285.

Kiresuk, T. J., & Lund, S. H. (1978). Goal attainment scaling. In C. C. Attkisson, W. A. Hargreaves & M. J. Horowitz (Eds), *Evaluation of human services programs* (pp. 341–369). New York: Academic Press.

Lambert, M. J., & Ogles, B. M. (2004). The efficacy and effectiveness of psychotherapy. In M. J. Lambert (Ed.), *Bergin and Garfield's handbook of psychotherapy and behavior change* (pp. 139–193). New York: Wiley.

Lazarus, R. S. (1991). *Emotion and adaptation*. New York: Oxford University Press.

Mannheimer, S., Friedland, G., Matts, J., Child, C., & Chesney, M. A. (2002). The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. *Clinical Infectious Diseases*, *34*, 1115–1121.

McDonald, H. P., Garg, A. X., & Haynes, R. B. (2002). Interventions to enhance patient adherence to medication prescriptions: Scientific review. *Journal of the American Medical Association*, *288*, 2868–2879.

Mergenthaler, E. (1996). Emotion-abstraction patterns in verbatim protocols: A new way of describing psychotherapeutic processes. *Journal of Consulting and Clinical Psychology*, *64*, 1306–1315.

Nieuwkerk, P. T., & Oort, F. J. (2005). Self reported adherence to antiretroviral therapy for HIV-1 infection and virologic treatment response: A meta-analysis. *Journal of Acquired Immune Deficiency Syndromes*, *38*(4), 445–448.

Orlinsky, D. E., & Howard, K. I. (1978). The relation of process to outcome in psychotherapy. In S. L. Garfield & A. E. Bergin (Eds), *Handbook of psychotherapy and behavior change: An empirical analysis* (2nd ed) (pp. 283–329). New York: Wiley.

Orlinsky, D. E., Rønnestad, M. H., & Willutzki, U. (2004). Fifty years of psychotherapy process-outcome research: Continuity and change. In M. J. Lambert (Ed.), *Bergin and Garfield's handbook of psychotherapy and behavior change* (pp. 307–390). New York: Wiley.

Paterson, D. L., Swindells, S., Mohr, J., Brestrer, M., Vergis, E. N., Squier, C., et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine*, *133*, 21–30.

Prochaska, J. O., DiClemente, C. C., & Norcross, J. C. (1992). In search of how people change: Applications to addictive behaviors. *American Psychologist*, *47*, 1102–1114.

Regli, D., & Grawe, K. (2000). *Der Berner Stundenbogen* [Post-session report]. Unpublished manuscript, University of Bern, Institute for Psychology.

Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: World Health Organization.

Schulte, D., Hartung, J., & Wilke, F. (1997). Handlungskontrolle der Angstbewältigung: Was macht Reizkonfrontationsverfahren so effektiv? [Action-control in coping with fear: What makes exposure so effective?]. *Zeitschrift für Klinische Psychologie. Forschung und Praxis*, *26*, 118–128.

Simoni, J. M., Frick, P. A., Lockhart, D., & Liebovitz, D. (2002). Mediators of social support and antiretroviral adherence among an indigent population in New York City. *AIDS Patient Care and STDs*, *16*, 431–439.

Stiles, B. (2002). Assimilation of problematic experiences. In J. C. Norcross (Ed.), *Psychotherapy relationships that work: Therapist contributions and responsiveness to patients* (pp. 357–365). London: Oxford University Press.

Taylor, S. E., & Brown, J. D. (1988). Illusion and well-being: A social psychological perspective on mental health. *Psychological Bulletin*, *103*, 193–210.

Turner, B. J. (2002). Adherence to antiretroviral therapy by human immunodeficiency virus-infected patients. *Journal of Infectious Diseases*, *185*(Suppl. 2), 143–151.

Wagner, G. J., Kanouse, D. E., Golinelli, D., Miller, L. G., Daar, E. S., Witt, M. D., et al. (2006). Cognitive-behavioral intervention to enhance adherence to antiretroviral therapy: A randomized controlled trial (CCTG 578). *AIDS*, *20*(9), 1295–1302.

Weber, R., Christen, L., Christen, S., Tschopp, S., Znoj, H. J., Schneider, C., et al. (2004). Effect of individual cognitive behaviour intervention on adherence to antiretroviral therapy: Prospective randomized trial. *Antiviral Therapy*, *9*, 85–95.

Willutzki, U. (1999). *Neue Version des Veränderungsfragebogens des Erlebens und Verhaltens von Zielke* [New version of the Questionnaire on Change of Experience and Behavior after Zielke]. Bochum, Germany: University of Bochum.

Zielke, M., & Kopf-Mehnert, C. (1978). *VEV—Veränderungsfragebogen des Erlebens und Verhaltens* [CEB—Questionnaire on Change of Experience and Behavior]. Weinheim, Germany: Beltz.

Znoj, H. J., Jeger, P., & Grawe, K. (2000). Die differentielle Bedeutung des Handlungskontrollmodus für klärungs- und bewältigungsorientierte Therapien [The differential role of the action-mode for clarification- and behavioral oriented therapies]. *Zeitschrift für Klinische Psychologie, Forschung und Praxis*, *29*, 52–59.

Znoj, H. J., Nick, L., & Grawe, K. (2004). Intrapsychische und interpersonale Regulation von Emotionen im Therapieprozess [Intrapsychic and interpersonal regulation of emotion in the therapeutic process]. *Zeitschrift für Klinische Psychologie und Psychotherapie*, *33*, 261–269.